REMARKS

THE AMENDMENTS AND REASONS FOR AMENDMENTS

Applicant amends claims 1, 3,15, 16, 21-23, 25, 37, 38, 43, and 44 and cancel claims 12-14, 18, 34-36, 40, 45, and 46. The amended claims add no new subject matter and are fully supported by the application, including the specification, examples, figures, and claims as originally filed.

For example support for the biological sample can be found on page 6, lines 26-29:

> The present invention relates to a sensitive method for the detection of a compound of interest present in a sample, such as a biological fluid, a biological extract, or an environmental sample, by means of a nucleic acid-labelled binding construct which is capable of recognizing and binding the compound of interest.

For example support for the specific binding of the recognition portion of the binding construct can be found on page 19, lines 13-19:

> In some embodiments, the binding of the recognition portion of the binding construct to the compound of interest may be both bivalent and bispecific (that is, the recognition portion may bind to and recognize two separate specific binding sites of the compound of interest). An example of a bivalent, monospecific binding is a dimeric antibody fragment or diabody (Holliger *et al.* (1993) *Proc. Natl. Acad. Sci. USA,* 90:6444-6448) that is designed to bind monospecifically. An example of a bivalent, bispecific antibody is a diabody that is designed to bind to two distinct binding sites of the compound of interest.

The amendments are made to clarify the claimed invention in order to expedite the allowance of the present application. Applicant reserves the right to file applications claiming the benefit of priority to the present application claiming the subject matter of the present and other applications.

For example support for the surfaces bearing specific binding targets capable of specifically binding to the recognition portion of the binding construct can be found in Example IV on page 29, lines 10-14:

Surfaces (magnetic particles) bearing accessible binding targets (Mopep2 peptides) bound any Fab-DNA not bound to the compound of interest, and a magnet was used to separate the surfaces, leaving the construct-compound complexes (Fab-DNA bound to antigen) in solution with the nucleic acid portion (pUC19) of the binding construct available for nucleic acid amplification.

APPLICANT'S CLAIMED INVENTION IS SUPPORTED BY THE SPECIFICATION UNDER 35 U.S.C. § 112(A), FIRST PARAGRAPH

The Examiner rejected claims 1-44 under 35 U.S.C. § 112, First Paragraph as allegedly not being supported by the specification. The Examiner alleges that in independent claims 1 and 23, the use of the phrase "non-nucleic acid" to describe the compound of interest and the recognition portion of the binding construct is not supported by the specification. Applicant respectfully disagrees with the Examiner that the specification does not define or describe the meets and bounds of the phrase "non-nucleic acid" however, in order to expedite the allowance of the claims, Applicant has amended independent claim 1 and 23 in order to more clearly claim the present invention. Applicant has amended the independent claims 1 and 23 to describe the recognition portion of the binding construct as comprising an antibody or an antibody fragment portion.

The Examiner alleges that in independent claims 1 and 23, the use of the phrase "essentially all" to describe the binding of the compound of interest with the binding construct and also the binding of the surfaces with unbound constructs is not supported by the specification. Applicant respectfully disagrees with the Examiner that the specification does not define or describe the meets and bounds of the phrase "essentially all" however, in order to expedite the allowance of the claims, Applicant has amended independent claim 1 and 23 in order to more clearly claim the present invention by deleting the phrase "essentially all."

APPLICANT'S CLAIMED INVENTION IS NOT OBVIOUS UNDER 35 U.S.C. § 103(A) IN VIEW OF THE REFERENCES CITED BY THE EXAMINER

The Examiner rejected claims 1-44 under 35 U.S.C. § 103(a) as allegedly being un-patentable

over Baez et al. (US Pat. No. 6,511,809) in view of Subramanian (US Pat. No. 5,244,816). The Examiner alleges that Baez et al. teach a method for detecting a compound of interest in a sample similar to the element of the claimed invention, except for addition of surfaces bearing non-nucleic acid binding targets for binding unbound binding constructs. The Examiner further alleges that the Subramanian's teachings makes up for the shortcomings of Baez et al. The Examiner, therefore, alleges that the claimed invention would have been obvious to one of ordinary skill in view of the cited references.

Applicant respectfully disagrees with the Examiner's characterization of the teachings of Baez et al. and Subramanian. Neither Baez et al. or Subramanian, separately or together, teach, suggest, motivate, or make obvious each and every elements of the claimed invention.

Applicant discussed the shortcomings of Baez et al. in Response to the previous Office Action, which Applicant incorporates herein by reference. Baez et al. or Subramanian, either separately or together do not teach each and every step of the claimed invention, in particular the present invention includes providing one or more surfaces bearing one or more accessible non-nucleic acid binding targets capable of specifically recognizing and specifically binding to the antibody or the antibody fragment portion of the binding construct. Baez et al or Subramanian do not report such surfaces bearing one or more accessible non-nucleic acid binding targets capable of specifically recognizing and specifically binding to the antibody or the antibody fragment portion of the binding construct.

Subramanian discloses methods for scavenging unbound metal labels from a reaction mixture for labeling biomolecules, wherein the biomolecules are bound through a chelator to a metal label and any unbound metal labels are removed from the reaction mixture by way of a chelator-matrix conjugate capable of binding the unbound metal labels. Subramanian discusses the removal of label from a sample of labeled bio-molecule in a process that yields a "purified" and labeled bio-molecule of interest by removing unused label. In contrast, the present invention is concerned with the binding characteristics of a previously labeled bio-molecule and not with a process that generates it. The present invention exploits these binding characteristics in the construction of a unique target molecule to remove bound from un-bound previously labeled bio-molecule, not the

isolation and purification of the bio-molecule itself. The present invention labels a bio-molecule with nucleic acid and these labeled, previously purified molecules are then utilized in a process to identify an analyte of interest in a biological sample. It is, therefore, not a purification process for the generation of a labeled molecule but rather a technological process used to identify the existence of a third party analyte from the separation of analyte-bound and unbound, labeled bio-molecules.

The purification process with scavenging by the use of chelators, as described by Subramanian, involves the binding and removal of labeling materials from a bio-molecule labeling process. Importantly, in the Subramanian reference, the chelating agent is selected to have high avidity and high affinity for a range of metals, whereas in the present invention, the binding targets of the surfaces have high avidity and high affinity for a complex, molecular structure and hence, have selective specificity, for example, for an antibody binding domain, an amino acid sequence, or carbohydrate moiety. The chelating agent, as described by Subramanian, has a wide range of specificity for many labels and the promiscuity of binding is an advantage in that context. One matrix will, therefore, bind to many different labels. In the present invention, however, fine specificity is required for label binding, and promiscuity is a disadvantage in this case. In the present invention, promiscuity will result in false-positive results. If specific binding of the antibody or antibody fragments of the present invention had a similar, wide range of specificity, as demonstrated by the chelating agents of Subramanian, then the binding of the binding construct of the present invention would render the technology useless. In other words, if the antibody or antibody fragment of the binding construct of the present invention, bound to many things, then molecules other than the analyte of interest or the binding targets of the surfaces would allow the binding construct to pass through the steps of the claimed invention resulting in false-positive assays.

Below, Applicant provides a formulaic representation of differences of the present invention (SAM Technology) compared to the disclosure of Subramanian reference:

A Subramanian

BM	Biomolecule to be labeled
L	label - metal or other inorganic compound not a biomolecule
A	Chelating Agent - inorganic or organic compound
M	Matrix for binding chelating agent

In cases where A is attached to both BM to grab label,L,
and also to remove excess L

(BM-A) + L

↓

(BM-A-L) + L

↓

add (M-A)

↓

(BM-A-L) + (M-A-L)

↓

remove (M-A-L)

leaves **(BM-A-L)** behind

B SAM Technology

BM1 or BM	Biomolecule to be labeled i.e the analyte of interest
L	label - binding construct (a biomolecule not an inorganic compound i.e. DNA-conjugated antibody)
BM2 or A	Mimetic also a biomolecule i.e. peptide or protein
M	Matrix for binding mimetic or "chelating agent"

In cases where A is attached to M to remove excess L

BM1 + L

↓

(BM1-L) + L

↓

add (M-BM2) or (M-A)

↓

(BM1-L) + (M-BM2-L)

↓

remove (M-BM2-L)

leaves (BM1-L) behind

In the SAM Technology

If BM1 is the same as BM2 in cases where the "mimetic" is the analyte of interest itself (BM1) attached to a matrix (as is the case in the Submaranian example) and the chelating agent is the same as the mimetic (that removes unbound label)

then A=BM1=BM2=BM

Then

A + L

↓

(A-L)' + L

↓

add (M-A)

↓

(A-L) + (M-A-L)

↓

remove (M-A-L)

leaves **(A-L) behind**
or BM1-L
or BM2-L
or BM-L

None of these is equivalent to the product in **A** which is **(BM-A-L)**

Therefore the example, closest in concept for the SAM Technology that was sited by the examiner, whereby the label is removed by a chelating agent identical to that on the biomolecule to be labeled and to that on the matrix to remove unbound label is not prior art for the SAM Technology ***BM-A-L is not equivalent to BM-L***

Based on the foregoing, Baez et al. and Subramanian, either separately or together, do not teach, suggest, or provide motivation to make the claimed invention obvious. Thus, the claimed invention is not obvious under 35 U.S.C. § 103(a). Accordingly, Applicant respectfully requests that this rejection be withdrawn.

Applicant respectfully submits that the claims are ready for examination and in condition for allowance.

Respectfully submitted,

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Date: 5 April 2006

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